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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,739	07/31/2001	William J. Egan	PHARMA.003A	3949

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EXAMINER

SMITH, CAROLYN L

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 04/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/919,739

Applicant(s)

EGAN ET AL.

Examiner

Carolyn L Smith

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3-8, 17 and 18 is/are pending in the application.
- 4a) Of the above claim(s) 17 and 18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3-8 is/are rejected.
- 7) ☒ Claim(s) 5 is/are objected to.
- 8) ☒ Claim(s) 3-8, 17 and 18 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Applicants' election without traverse of Group II (claims 3-8), the cancellation of claims 1-2 and 9-16, and the addition of new claims 17 and 18 in Paper No. 4, filed 1/22/03, are acknowledged.

Claims 17 and 18 are withdrawn from consideration because these claims are of the type of cancelled claim 1, which is in a different restriction Group from claims 3-8 as indicated in the Action, mailed 12/17/02. Claim 17 and its dependent claim 18 are directed to non-elected subject matter including "predicting" and "at least one property."

The restriction requirement is deemed proper and is therefore made FINAL.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to activity prediction models whereas in contrast the elected claims include a method of selecting a set of marker molecules for structural comparisons in a model for molecular behavior prediction.

Claims herein under examination are 3-8.

Specification

The disclosure is objected to because of the following informality: the presence of a double period on page 4, line 14. Appropriate correction is required.

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Claim Objections

Claim 5 is objected to because of the following informality: on line 15, the adjective “fractions-correctly predicted” lacks an appropriate noun, such as “metric”. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 3-8 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to a mathematical algorithm which is considered non-statutory subject matter. As stated in the MPEP § 2106 IV(B)(1):

If the “acts” of a claimed process manipulate only numbers, abstract concepts or ideas, or signals representing any of the foregoing, the acts are not being applied to appropriate subject matter. *Schrader*, 22 F.3d at 294-95, 30 USPQ2d at 1458-59. Thus, a process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus cannot constitute a statutory process.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The

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factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF ENABLEMENT

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 8, lines 3-5, relates to choosing one of the preliminary sets which “most accurately predicts molecular behavior” as the final set of marker molecules. The specification does not provide enablement for the practice of claim 8 of what is performed to result in this choosing of the final set.

Due to the lack of direction/guidance presented in the specification regarding determination of the final set which “most accurately predicts molecular behavior” and the absence of working examples directed to the same, the specification fails to teach the skilled artisan how to make and use the claimed invention regarding claim 8.

Claims Rejected Under 35 U.S.C. § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claim 3, line 4, recites the limitation "the at least one property". There is insufficient antecedent basis for this limitation in the claim. Claims 4-8 are also rejected due to their direct or indirect dependence from claim 3.

Claim 8 recites the phrase "most accurately predicts" (line 4) which is vague and indefinite. It is unclear what criteria are required to be considered the most accurate of all predictions. Clarification of this phrase via clearer claim wording is requested.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Stanton et al. (J. Chem. Inf. Comput. Sci. 1999, Vol. 39, pages 21-27).

Stanton et al. disclose that the objective of drug discovery screening programs is to identify hits, or a selection of molecules, to provide a preliminary understanding of the structure-activity relationship between a set of compounds and a target (page 21, col. 1, lines 1-15).

Stanton et al. disclose the necessity of the program to evaluate large databases (sets) with

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molecular descriptors in order to select those that produce chemistry spaces general enough to study large and diverse subsets of chemical structures and still be able to identify subtle differences between highly similar substances (page 21, col. 1, lines 25-33). Stanton et al. disclose programs which identify leads for potential drug candidates (abstract, lines 1-2). For example, Stanton et al. disclose subsets of a set of compounds from a larger combinatorial library used in assays to identify compounds with antibacterial activity (page 22, col. 2, lines 11-28). Thus, the hits in these subsets function as molecular markers which are reasonably interpreted as things that mark or indicate a concept or trait, such as antibacterial activity (page 22, col. 2, lines 13-14). Stanton et al. disclose examples of various properties to examine involving protein binding such as inhibition of bacterial cell growth, metabolic pathways, and isolated enzymes (page 23, col. 2, lines 1-5) so that selected molecules which indicate the presence of these properties would be considered markers of the properties. As mentioned above, Stanton et al. disclose an example of using the property of antibacterial activity (page 22, col. 2, lines 11-14) in a study, starting with a large combinatorial library (10,000 compounds), finding 212 hits (which represents the classification of a set of reference molecules as stated in claim 3), performing a hierarchical cluster analysis (Figure 1), using a cutoff point (threshold) to yield seven subsets (which represents subset selection as stated in claim 3), and then conducting further studies on representatives in the subsets (which represents the selection of marker molecules from the subset in claim 3) (page 22, col. 2, lines 10-28). Stanton et al. disclose the use of molecular and biological descriptors when doing cluster analysis (page 22, col. 1, lines 16-24). Stanton et al. disclose cluster analysis resulting in dendrograms which were examined visually to determine cut-off thresholds for appropriate levels of similarity (page 21, col. 2, lines

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24-26 and Figure 1) to further narrow down the selection of molecules as stated in claim 3.

Stanton et al. disclose the goal of producing sufficient data for each class of hits (subsets) to make decisions regarding potential leads (page 21, col. 1, lines 15-18 and page 22, col. 2, line 1), such that selection of the potential leads within the subset are the selected marker molecules as stated in claim 3. Stanton et al. disclose the cluster analysis methods provide a rapid way to reducing large sets of hits into smaller manageable structural classes (page 22, col. 2, lines 1-5).

Stanton et al. disclose an example where three subsets were clearly visible in the resulting dendrogram (page 22, col. 2, lines 29-41 and Figure 2) from which compounds were selected for follow-up work from each class as stated in claim 3. Stanton et al. disclose the molecular structure descriptors were taken from BCUT metrics which form a particular chemistry space in order to perform hierarchical cluster analysis, including a similarity metric which was predefined to be based on the squared Euclidean distance (page 21, col. 2, lines 9-23) as stated in claim 5.

Stanton et al. disclose the activity of five related hits and each compound's Euclidean distance from the original query (page 24, col. 1, lines 37-41). Stanton et al. disclose nearest-neighbor (NN) searches (page 21, col. 2, lines 27-29) that included the query compounds as well as the compounds from databases to calculate BCUT metrics (page 22, col. 1, lines 1-3). Stanton et al. disclose the 20-30 closest neighbors to a given query were selected from multiple databases for subsequent screening (page 22, col. 1, lines 4-5) which is reasonably interpreted that the counting step was repeated producing varying results (20-30 results) as stated in claim 5. Stanton et al. disclose that the hit rate can be controlled by altering assay conditions used or setting rigorous criteria of a specific property (i.e. 80% inhibition instead of 50%) as well as looking at a broad range of hits (page 22, col. 1, lines 32-36) which is reasonably interpreted as repeating the count

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process with various thresholds as stated in claims 5, 6, and 7. Stanton et al. disclose some subsets at 100% similarity in Figure 2 which represent a minimum distance as well as the most accurate of predictions as seen in the dendrogram as stated in claims 7 and 8. Stanton et al. disclose the final six best hits (markers) out of 210 compounds, which represent the most accurate hits from the original subset (Table 1 caption). Stanton et al. disclose an example of nearest neighbor analysis of a first molecule that is used to identify sets of potentially active compounds that are similar to the first molecule (page 24, col. 1, lines 29-37 and Table 1). Stanton et al. disclose in Figures 5a and 5b the sorting of molecules (210 total, see Table 1 caption) in a set in descending order of numerical similarity (based on Euclidean distance) to the original query where one can visually determine the number of molecules in between the first molecule and another molecule at a particular NN distance away as stated in claim 5. Stanton et al. disclose using active compounds as starting points to screen other compounds for similarity using a threshold of $\leq 50 \mu\text{M}$ as the threshold cut off value (page 24, col. 2, lines 8-16). Stanton et al. disclose a fractions-correctly-predicted metric in Table 2 (last column) where the number of molecules in the range which are also part of the subset (third column) are divided by the total number of molecules in the range (second column) to give the metric expressed as a percent in the fourth column (page 25, col. 1-2 and Figure 5). Stanton et al. disclose a threshold of a NN distance of 1.9 or less in order to find a 20% hit rate (page 26, col. 1, lines 6-11).

Thus, Stanton et al. anticipate the limitations in claims 3-8.

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Conclusion

No claim is allowed.

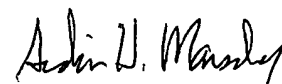
Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (703) 308-6043. The examiner can normally be reached Monday through Friday from 8 A.M. to 4:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

March 31, 2003


ARDIN H. MARSCHEL
PRIMARY EXAMINER